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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/103,355	06/23/1998	PETER J. KUSHNER	2307O-080510	2899

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EXAMINER	
PAK, MICHAEL D	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 03/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

HL

Office Action Summary	Application No.	Applicant(s)	
	09/103,355	KUSHNER ET AL.	
	Examiner	Art Unit	
	Michael Pak	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 September 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Amendment filed September 20, 2004 has been entered.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Applicant's arguments filed 20 September 2004, have been fully considered but they are not found persuasive.

Claim Rejections - 35 USC § 112

4. Claims 1-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recite the term "estrogen receptor different from said cognate receptor" whose metes and bounds are not clear. It is not clear when an estrogen receptor is not an estrogen receptor. For example, if the cognate receptor is one species of estrogen receptor then is an estrogen receptor which is a fusion protein different from the cognate receptor which is an estrogen receptor.

Claim Rejections - 35 USC § 102

5. Claims 1-5, and 7-11 are rejected under 35 U.S.C. 102(e) as being anticipated by Kushner et al.((AB); U.S. 5,723,291).

The teachings of Kushner et al. has been set forth in the previous office actions. The previous rejection has been reinstated because Kushner et al. teach a method with a cell or cells which express the estrogen receptors, fos, jun, and AP-1 promoter fused to CAT gene ((columns 4-8, 10-12, and 17-20). The cells were contacted with estrogen which resulted in detection of the reporter CAT (column 10). The limitation of cognate receptor is generic and encompasses additional estrogen receptors or fos and jun proteins in the cell. Page 6, lines 1-2, defines nuclear transcription ligand as a compound that binds to a nuclear transcription factor thus both fos and jun are nuclear receptors and ligands because they are transcription factors and they bind to each other. The definition of "cognate receptor" in the specification on page 6, lines 13-14, does not further limit claim than the receptor in claims 2 and 3. Furthermore, different ligands were tested simultaneously in figures 10-12 which meets the limitations of the claimed ligand. The newly amended claim limitations for the negative control is taught by transfection with or without jun or fos at the same time or singly (columns 10 and 13). Furthermore, Kushner et al. teach a method using MDA453 cells (columns 5, 14 and 15) which express endogenous estrogen receptor by transfecting with estrogen receptor fusion protein (columns 13-15). The estrogen receptor fusion protein is not excluded by the term "cognate receptor" or "estrogen receptor" and the ligands are estrogens and antiestrogens. The assays are performed with and without hormones (columns 13-15). Both fos and jun are in the methods of the assays in order for the AP-1 sites to work

and thus are in contact with the cells. The cells are co-transfected with both estrogen receptor and Jun/Fos (column 13). The jun in the cell is c-jun (column 10). There are more than one cell in the assay.

6. Claims 1-13 are rejected under 35 U.S.C. 102(e) as being anticipated by Evans et al.((B); U.S. 5,639,592) with evidence from Kushner et al.((AB); U.S. 5,723,291).

Evans et al. teach the method using a cell (such as HeLa, CV-1, NIH-3T3 cells; column 8) comprising c-jun, fos (column 5), and nuclear receptors (such as glucocorticoid, retinoic acid, estrogen, androgen, progesterone, vitamin D3, mineralcorticoid receptors; columns 6, 8-16). The column 7 teaches the method using AP-1 proteins by exogenous expression. Furthermore, column 5 teaches the method using AP-1 proteins endogenously or by administering fos or jun. Column 6 teaches the method using the estrogen receptor. The pages 7-8 of the specification's definition of "AP-1 mediated estrogen activity" is generic to the teachings of Evans et al. and does not exclude the teachings of Evans et al. Kushner provide evidence that HeLa, CV-1, and NIH-3T3 cells inherently express estrogen receptor (column 12, Table I). Thus, claim 1 limitations are met. Claim 2 requires a second cell and assays were performed with more than one cell in a cell culture which comprises the all the elements of the first cell which meet the limitations of claim 2. The term "transcription factor ligand" as defined is a generic term and does not exclude fos and jun because fos and jun are transcription factors which bind and thus are receptors as well. Claim 3 limitation is that the cells are the same which is met above. Claims 4 and 5 definition of "cognate

receptor" in the specification on page 6, lines 13-14, does not further limit claim than the receptor in claims 2 and 3.

7. Claims 1-2, 4, 8, and 10-11 are rejected under 35 U.S.C. 102(e) as being anticipated by Pfahl et al.((A); U.S. 6,004,748) with evidence from Kushner et al.((AB); U.S. 5,723,291).

Pfahl et al. teaching was set forth in the previous office actions.

Pfahl et al. teaches a method of detecting AP-1 interaction with cell containing estrogen receptors and as well as AP-1 promoter (columns 1-3 and 7-8). Columns 2 and 4 teaches the method using AP-1 proteins, cJun and cFos, by exogenous expression. Furthermore, column 2 teaches the method using AP-1 proteins endogenously expressing fos or jun. Column 2 teaches the method using the estrogen receptor. The pages 7-8 of the specification's definition of "AP-1 mediated estrogen activity" is generic to the teachings of Pfahl et al. and does not exclude the teachings of Pfahl et al. including effects of dexamethasone. Kushner provide evidence that HeLa, CV-1, and NIH-3T3 cells inherently express estrogen receptor (column 12, Table I).

Page 6, lines 1-2, defines nuclear transcription ligand as a compound that binds to a nuclear transcription factor thus both fos and jun are nuclear receptors and ligands because they are transcription factors and they bind to each other. The definition of "cognate receptor" in the specification on page 6, lines 13-14, does not further limit claim than the receptor in claims 2 and 3.

Claim Rejections - 35 USC § 103

8. Claims 1-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kushner et al.((AB); U.S. 5,723,291) in view of Pfahl et al.((A); U.S. 6,004,748), Evans et al.((B); U.S. 5,639,592), GAUB et al.((AV); Cell, 1990), Webb et al.(CB) and Kushner et al.((AD); WO 95/06754).

The teachings of Kushner et al.((AB); U.S. 5,723,291) Pfahl et al.((A); U.S. 6,004,748), and Evans et al.((B); U.S. 5,639,592), have been discussed above.

GAUB et al. teach a method using the cell comprising estrogen receptor, ovalbumin element which is target for transactivation by c-fos and c-jun linked to CAT reporter(page 1271 and figure 6). Cells are contacted with TPA or forskolin and the receptor(HE0) and fos and jun and reporter activity measured (page 1271 and figure 6). Page 6, lines 1-2, defines nuclear transcription ligand as a compound that binds to a nuclear transcription factor thus both fos and jun are nuclear receptors and ligands because they are transcription factors and they bind to each other. TPA and forskolin activates the cell thus are compounds which have AP-1 mediated estrogenic activity. A second cell and figure 6 were performed with more than one cell in a cell culture which comprises the all the elements of the first cell . Limitation that the cells are the same which is met above. Claims 4 and 5 definition of "cognate receptor" in the specification on page 6, lines 13-14, does not further limit claim than the receptor in claims 2 and 3.

Webb et al.(CB) and Kushner et al.((AD); WO 95/06754) are cumulative reference with Kushner et al.((AB); U.S. 5,723,291) Pfahl et al.((A); U.S. 6,004,748), Evans et al.((B); U.S. 5,639,592), and GAUB et al.((AV); Cell, 1990).

Claims 6 and 7 recite specific Markush group of ligands and cognate receptors, respectively, which are not taught by Kushner et al.((AB); U.S. 5,723,291).

It would have been obvious to modify the method of Kushner et al.((AB); U.S. 5,723,291) by incorporating the teaching of Pfahl et al.((A); U.S. 6,004,748), Evans et al.((B); U.S. 5,639,592), and GAUB et al.((AV); Cell, 1990) and further use the glucocorticoid receptor, retinoic acid receptor, or other nuclear receptors. One of skilled in the art would have been motivated combine the teaching of the references because they are analogous references which teach nuclear receptors interaction with AP-1 site and AP-1 protein interaction. Further motivation is provided by Evans et al. who teach that understanding the mechanism of the regulatory effect of hormones, receptors, and AP-1 transcription factors are important to determine undesirable side effects especially as it relates to proto-oncogenic effects of cell growth and differentiation (columns 1 and 2). Evans et al. motivation is especially important in view of the regulatory interaction of estrogen signalling pathway with glucocorticoid, progestins, and androgens as taught by Gaub et al. (Pages 1267 and 1273). Further motivation is provided by Pfahl et al. who teach that methods of the invention can be used to identify and screen new ligand of nuclear receptor useful for treatment of cancer because the receptors (such as estrogen and glucocorticoid etc.) interaction with AP-1 (columns 1-3).

Double Patenting

9. Claims 1-13 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-27 of U.S. Patent No.

5,723,291 in view of Pfahl et al.((A); U.S. 6,004,748), Evans et al.((B); U.S. 5,639,592), GAUB et al.((AV); Cell, 1990), Webb et al.(CB) and Kushner et al.((AD); WO 95/06754). Although the conflicting claims are not identical, they are not patentably distinct from each other.

The teachings of Pfahl et al.((A); U.S. 6,004,748), Evans et al.((B); U.S. 5,639,592), GAUB et al.((AV); Cell, 1990), Webb et al.(CB) and Kushner et al.((AD); WO 95/06754) are discussed above.

It would have been obvious at the time of the invention to modify the method of claims 1-27 of U.S. Patent No. 5,723,291 by incorporating the teaching of Pfahl et al.((A); U.S. 6,004,748), Evans et al.((B); U.S. 5,639,592), and GAUB et al.((AV); Cell, 1990) and further use the glucocorticoid receptor, retinoic acid receptor, or other nuclear receptors. One of skilled in the art would have been motivated combine the teaching of the references because they are analogous references which teach nuclear receptors interaction with AP-1 site and AP-1 protein interaction with interests in understanding cancer cell growth regulation. Further motivation is provided by Evans et al. who teach that understanding the mechanism of the regulatory effect of hormones, receptors, and AP-1 transcription factors are important to determine undesirable side effects especially as it relates to proto-oncogenic effects of cell growth and differentiation (columns 1 and 2). Evans et al. motivation is especially important in view of the regulatory interaction of estrogen signalling pathway with glucocorticoid, progestins, and androgens as taught by Gaub et al. (Pages 1267 and 1273). Further motivation is provided by Pfahl et al. Wwho teach that methods of the invention can be used to identify and screen new

ligand of nuclear receptor useful for treatment of cancer because the receptors (such as estrogen and glucocorticoid etc.) interaction with AP-1 (columns 1-3).

10. No claims are allowed.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Pak whose telephone number is 571-272-0879. The examiner can normally be reached on 8:30 am - 2:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 571-272-0829. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9306 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-0507.

Michael D. Pak

Michael Pak
Primary Examiner
Art Unit 1646
1 March 2005